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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,071	01/09/2006	Zeev Smilansky	85189-16500	2101

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WINSTON & STRAWN LLP
PATENT DEPARTMENT
1700 K STREET, N.W.
WASHINGTON, DC 20006

EXAMINER	
BORIN, MICHAEL L	
ART UNIT	PAPER NUMBER
1631	

NOTIFICATION DATE	DELIVERY MODE
09/14/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@winston.com
mwalker@winston.com

Office Action Summary	Application No.	Applicant(s)	
	10/537,071	SMILANSKY, ZEEV	
	Examiner	Art Unit	
	Michael Borin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *109-121* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *109-121* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/06/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/06/2009 has been entered.

Status of Claims

1. All previously pending claims are canceled. New claims 109-121 are added.

Claim Rejections - 35 USC § 112, second paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 109-121 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter

which applicant regards as the invention. The rejection is applied for the following reasons.

A. The claims are directed to use of "at least one" labeled tRNA. It is not clear how labeling one tRNA, e.g., $tRNA^{Ala}$ allows identifying identity of polypeptide comprised of a plurality of types of amino acids. In other words, while a FRET signal from $tRNA^{Ala}$ would indicate progression of peptide synthesis in general, it is unclear how it will assist in identifying identity of polypeptide comprised of a plurality of types of amino acids.

B. Claim 109: the claim addresses a "database compiled from signal data". It is not clear what signal data are used in the compilation of the database, and how the interrogation is being carried out.

Claim Rejections - 35 USC § 112, first paragraph.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 109-121 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The claims address monitoring and identifying a protein (or a plurality of proteins) being synthesized in a ribosome by detecting signals from labeled roibosome and labeled tRNA and **interrogating a database compiled from signal data** so as to identify the one or more proteins.

Thus, the claims require a database compiled from signal data in order to be able to identify the one or more proteins. However, the specification does not demonstrate that applicant is in possession of such a database, nor it demonstrates identifying nature of a protein using such a database. Instead, specification describes, in general, desirable features of a database that can be created – see p. 68, lines 7-27 , which is not a sufficient demonstration that applicant was in possession of such desirable database at the time of filing. Further, the database discussed in the said section of specification is not "a database compiled from signal data" (i.e., per claim, "from signals emitted when the two labels are in proximity"), but rather to a database of annotated sequences:

...the database has to be compiled. Every protein sequence is simply transformed to a label sequence by marking each amino acid as "N" of"F" according to whether its synthesis will result in a FRET signal or not.

p. 68, lines 7-12

Nor there is a description of identifying of one or plurality of proteins being synthesized using such database compiled from signal data; rather, in the demonstration of data analysis, applicant uses an exemplary peptide composed of amino acid residues F and N, i.e., generic residues marked to indicate whether residue's synthesis will result in a FRET signal or not, rather than demonstrates identifying nature of a protein, i.e., a polypeptide comprised of hundreds of residues and potentially having 20 types of amino acid residues.

The art provides teaching of using FRET fluorescence signals from combination of signals from labeled ribosomes and tRNAs to study the mechanisms of protein synthesis in ribosomes, but not to identify the nature of a protein being synthesized (see references used in the art rejections of record).

The inventor must be able to describe the item to be patented with such clarity that the reader is assured that the inventor actually has possession and knowledge of the unique method that makes it worthy of patent protection. The reader can certainly appreciate the goal but establishing goals does not make a patent. As the Court of Appeals for the Federal Circuit stated in a case involving similar issues, an inadequate patent description that merely identifies a plan to accomplish an intended result "is an attempt to preempt the future before it has arrived." *Fiers v. Revel*, 984 F.2d 1164, 1171 (Fed. Cir.1993). To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. *Vas-Cath*, 935 F.3d at 1563; *see also Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"). There is no demonstration in the specification that applicants generated any instructions which would allow identify a polypeptide and at least three molecular structures capable of associating with it that would produce a complex having an unidentified inhibitory character. Similarly to *In re Wilder*, 736 F.2d 1516 (Fed. Cir. 1984), *cert. denied*, 469 U.S. 1209 (1985) the

specification did "little more than outline goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."

Section 112, first paragraph, requires the patentee to "show that an invention is complete by disclosure of substantially detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the invention. Even if the inventors were reasonably certain that a database compiled of FRET signal data can be used to identify proteins being synthesized in ribosomes, there is no showing in the patent that they knew to be a fact that such a database would be sufficient for the stated objective. The reader can certainly appreciate the goal but establishing goals does not make a patent. An inadequate patent description that merely identifies a plan to accomplish an intended result "is an attempt to preempt the future before it has arrived." *Fiers v. Revel,* 984 F.2d 1164, 1171 (Fed. Cir.1993).

Based on these factors, those of ordinary skill in the art of protein biosynthesis would not recognize that the inventor to have been in possession of the claimed method as claimed at the time of filing.

Claim Rejections - 35 USC § 103.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4 Claims 109-121 are rejected under 35 U.S.C.103(a) as unpatentable over Odom (Biochemistry, 1990 Dec 4; 29(48):10734)

The instant claims are drawn to method for monitoring protein synthesis comprising

- binding a first label to at least one ribosome or a fragment thereof;
- binding a second label to at least one tRNA;
- detecting electromagnetic radiation signals emitted when the first and second labels are in proximity, the signals indicating progression of the synthesis of the one or more proteins; and
- analyzing the detected signals to identify one or more proteins being synthesized by interrogating a database compiled from signal data so as to identify the one or more proteins that most likely have produced the detected signals

Odom et al teach method comprising

- binding a first label to at ribosome, e.g., at S21 or L1 protein;
- binding a second label to $tRNA^{Phe}$;

- detecting FRET fluorescence signal electromagnetic radiation signals emitted when said labels are in proximity, wherein such FRE signal indicates progression of protein synthesis; and
- analyzing the detected signals

Odom does not teach identifying sequence of nascent peptide; however, the phrase "so as to identify the one or more proteins that most likely have produced" is broadly interpreted as to identify the event that one or more proteins are being have produced; the reference does identify the fact of nascent peptide being synthesized.

Odom doers not teach interrogating a database compiled from signal data. However, implicitly, the reference does teach referring to database information because to decipher a nature of fluorescence signals, i.e., excitation, emission, and quenching, one would need to know characteristics of the given fluorescent labels< such as FM or FITC or AETUC labels used in Odom, and such characteristics can be viewed as a database information, available in databases of fluorescent labels. Therefore, it would be obvious to one skilled in the art to be motivated to use such database information is interpreting fluorescent signals in Odom.

With respect to dependent claims 110-121 if there are any differences between Applicant's claimed method and that of the prior art, the differences would be appear minor in nature. Although the prior art do not teach the various combinations of signal acquisition and analysis as claimed, the nature of the problem to be solved – monitoring protein synthesis in ribosomes - would lead inventors to look at references relating to possible factors known to affect detection and identification of fluorescent signals of

labeled ribosome components. Based on particular situation, it would be conventional and within the skill of the art to select and/or determine such result-oriented variables as appropriate labeling sites (such as particular ribosome proteins addressed both in Odom and instant claims 96,97), conditions for signal measurement and acquisition (e.g., single *vs.* plural ribosomes, measuring after preliminary irradiation, using FRET conditions, etc), as well as signal analysis (e.g., recording signal type and comparing to database information, finding matching database information, etc). One of ordinary skill in the art would have been motivated to combine all known factors with no change in their respective functions, and the combination would have yielded nothing more than predictable results of more comprehensive monitoring of protein synthesis.

Art of record

5. Puglisi et al (US 20040023256; effective filing date 01/27/2003) teach methods of determining translational profile using ribosome complexes are immobilized on a solid surface. One or more components of the surface-bound ribosome complex may be labeled at specific positions to permit analysis of multiple or single molecules for determination of ribosomal conformational changes and translation kinetics. tRNAs and ribosomes (e.g. ribosome protein S21) are labeled with fluorescent labels and their interaction is monitored by measuring FRET signal. See paragraphs [0019], [0062]-[0068], Example 3. The translation profile can be used to identity of the polypeptide product. See Abstract, paragraphs [0012],[0014]. The translation profile may be compiled and compared with a database of reference translation profiles. Such

databases may include reference translation profiles from defined biological samples. See paragraphs [0021],[0022],[0077].

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Borin, Ph.D./
Primary Examiner, Art Unit 1631